Prioritizing the evaluation of HIV prevention interventions in pregnancy: Interim results from a randomized, open-label safety trial of dapivirine vaginal ring and oral tenofovir disoproxil fumarate/emtricitabine use in late pregnancy

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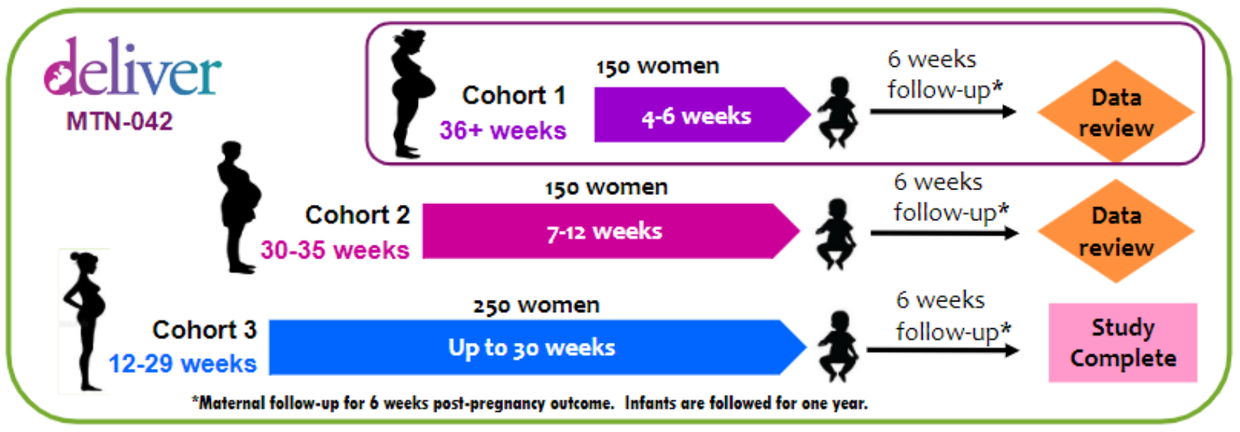
Background

- The monthly dapivirine vaginal ring (DVR) has been clinically shown to reduce HIV risk with a favorable safety profile in non-pregnant reproductive-aged women[1,2]
- The WHO recently recommend DVR for use among women at increased risk of HIV acquisition;[3] however, safety data on use during pregnancy are lacking
- Here we report interim safety data from the first cohort of pregnant participants in MTN-042/DELIVER, a phase IIIb, randomized, open-label safety trial of DVR and oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC)
  (ClinicalTrials.gov number: NCT03965923)



Analysis Objective

- To assess maternal & infant safety associated with product use during pregnancy in **Cohort 1**

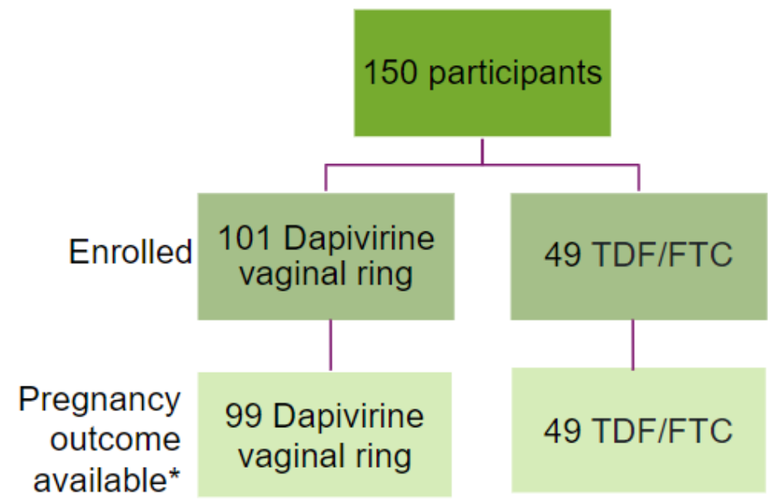
Methods

- Eligible women aged 18 to 40 in Blantyre, Malawi; Johannesburg, South Africa; Kampala, Uganda and Chitungwiza, Zimbabwe were randomized 2:1 to monthly DVR or daily TDF/FTC
- Participants initiated product use between 36 0/7-37 6/7 weeks' gestation and continued until delivery or 41 6/7 weeks gestation
- Pregnancy outcomes and complications reported at the time of delivery were assessed and summarized using descriptive statistics and compared to local background rates obtained through a chart review (MTN-042B)[4]

In this first study of a long-acting HIV prevention agent used in pregnancy, adverse pregnancy outcomes and complications were uncommon when the dapivirine vaginal ring and tenofovir disoproxil fumarate/emtricitabine were used in late pregnancy and were generally similar to rates observed in the communities where the study is being conducted.

Results

Figure 1. CONSORT Diagram



*1 participant was lost to follow-up following their Week 1 Phone Contact visit' 1 participant withdrew consent after randomization but prior to study product administration

- One-hundred and fifty participants were enrolled with 101 randomized to DVR and 49 to TDF/FTC
- Median age was 25 years (interquartile range [IQR] 21-28), 31% reported a prior pregnancy, and median gestational age at enrollment was the same in both arm (36.3 weeks (IQR 36, 37))

Table 1. Pregnancy outcomes by study arm

	Dapivirine n=99 n (%)	TDF/FTC n=49 n (%)	Overall N=148 N (%)
Stillbirth	0 (0)	1 (2)	1 (1)
Live birth	99 (100)	48 (98)	147 (99)
Full term birth	98 (99)	46 (96)	144 (98)
Preterm birth	1 (1)	2 (4)	3 (2)

Figure 2. Percent of participants enrolled at each site

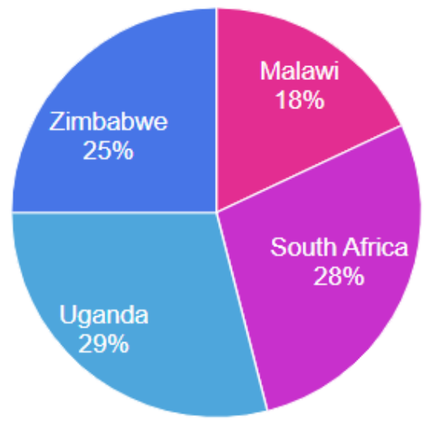


Table 2. Maternal pregnancy complications by study arm[1]

	Dapivirine n=99 n (%)	TDF/FTC n=49 n (%)	MTN-042B frequencies[2] % (95% CI)
Any hypertensive disorder of pregnancy[3]	3 (3)	4 (8)	10.6% (10.0, 11.3)
Gestational hypertension	3 (3)	2 (4)	4.4% (4.0, 4.8)
Pre-eclampsia without severe features	0 (0)	1 (2)	2.2% (1.9, 2.5)
Pre-eclampsia with severe features	0 (0)	1 (2)	2.1% (1.9, 2.4)
Eclampsia	0 (0)	0 (0)	0.6% (0.5, 0.8)
Hemorrhage			
Peripartum/Antepartum hemorrhage	0 (0)	1 (2)	--
Postpartum hemorrhage	2 (2)	1 (2)	3.2% (2.9, 3.6)

[1]Other complications assessed included: chorioamnionitis, puerperal sepsis, endometritis, preterm premature rupture of membranes, and fever of unclear etiology.
[2]Data on background rates obtained as part of a published systematic chart review (MTN-042B).
[3]Participants may experience more than one form of hypertensive disorder in pregnancy, therefore the sum of the rows may be higher than the total number of participants in this row.

- Nearly all pregnancies resulted in a live birth and the majority were full term, as expected based on Cohort 1 eligibility criteria (**Table 1**)
- Pregnancy complications were rare, with hypertensive disorders being the most common complication reported (**Table 2**)

Severe Adverse Events (SAEs)

Maternal SAEs

- Of the SAEs/grade ≥3 AEs reported, only one AE (grade III nausea) was deemed related to study product use in the TDF/FTC arm

Infant SAEs

- There were no infant SAEs/grade ≥3 AEs related to study product
- At the time of this report, there was one neonatal death following delivery in the TDF/FTC arm

Conclusions

- In this first study of a long-acting HIV prevention agent in pregnancy, adverse pregnancy outcomes and complications were uncommon when the DVR and TDF/FTC were used in late pregnancy and were generally similar to rates observed in the communities where the study is being conducted
- These data support plans for subsequent investigation of safety among pregnant women using DVR earlier in pregnancy

References
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We are immensely grateful to the pregnant individuals and their infants who are participating in the DELIVER study.

The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068633, UM1AI068615, UM1AI106707), with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. The vaginal rings used in this study were developed and supplied by the International Partnership for Microbicides (IPM). Oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was donated by Gilead Sciences.

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IAS 2021 18 –21 July